

CONSENT FORM**Subject Name** _____

Title of Protocol A randomized placebo-controlled double blind trial of liraglutide 3mg [Saxenda] on weight, body composition, hormonal and metabolic parameters in obese women with polycystic ovary syndrome (PCOS)

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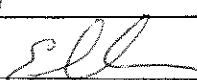
Sponsoring Agency: Novo Nordisk A/S

Please read this form carefully. This consent form contains important facts to help you decide if it is in your best interest to take part in this study. Take time to ask the study doctor or study staff as many questions about the study as you would like. If there are any words or information that you do not understand, please ask the doctor. The study doctor or study staff will explain them to you. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in the research study, you must sign your name to the final page. Your taking part is entirely voluntary.

Purpose of the Study

You are being asked to take part in a clinical research study because you have a disorder called polycystic ovary syndrome (PCOS). Women with PCOS have a hormonal imbalance and metabolism problems that can bring about irregular menstrual cycles, excess hair growth, and weight gain. Treatment for PCOS focuses on managing your specific concerns such as difficulty losing weight and includes lifestyle changes (diet and exercise) and drug therapy. This study is being done to determine the ability of the medicine liraglutide 3mg (Saxenda) in combination with a healthy lifestyle to cause weight loss and improve metabolic and reproductive function in women with PCOS. The medicine is administered as a subcutaneous (under the skin) shot that you can give to yourself once a day. This medicine will be either liraglutide 3mg (Saxenda) or placebo (a liquid that looks the same but has no drug in it). The effects of the liraglutide 3mg (Saxenda), both good and bad, will be compared to the placebo. You will need to take one of

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the injectable medicines for about 30 weeks. Liraglutide 3mg (Saxenda) is approved by the U.S. Food and Drug Administration (FDA) as a weight loss drug.

Seventy-two women with PCOS will take part in the study at The Woman's Hospital in Baton Rouge, Louisiana. The length of time you will be in this study is about 32 weeks.

If you volunteer to take part in this research study, you will be asked to read and sign this consent form. You will then provide information about the following.

- your reproductive history
- a medical history
- height and weight
- menstrual bleeding cycle length
- race
- current drug use
- cigarette smoking/tobacco use
- alcohol intake

If you are eligible to take part in the study and you meet the medical conditions, you will be placed to one of two treatment groups:

- liraglutide 3mg (Saxenda)
- liraglutide 3mg placebo

Your treatment will be chosen on a **randomized** basis, which is similar to rolling dice. A computer will choose which of the medicines you will get. One group of women get the injectable study drug. A second group of women will get an injectable placebo (liquid with no drug in it). The computer will put you in a group by chance. You have 2 chances of getting the study drug compared to one of getting the placebo drug. Neither your doctor nor you will be able to choose which treatment you will be given. The study staff and the women who take part **will not know** which group is getting the study drug or placebo.

Once you have enrolled and been randomized to study drug, you will be taught how and when to take the medicine. You will be instructed to take the medicine once a day at about the same time every day. Before starting treatment with the injectable medicine, you will be trained how to use the pre-filled injection (shot) pen. All subjects (liraglutide 3mg or placebo group) will receive this training. The clinic nurse will also see you about 16-18 weeks after starting the study drug to find out how you are tolerating the medicine. At that time, the study coordinator will dispense new medicine. If there are any questions about the medications and how to take them, you can call the Woman's Weight Loss and Metabolic Clinic at 225 924-8947 or the Research Office at 225 231-5275.

Procedures during the Study

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You will have a total of 5 visits over a 32-week period. The visits are as follows:

- Visit 1: baseline outpatient laboratory visit / DEXA scan in radiology (week 1)
- Visit 2: first clinic visit (week 2)
- Visit 3: outpatient laboratory and clinic visit (week 16-18)
- Visit 4: final outpatient laboratory visit / DEXA scan in radiology (week 30-32)
- Visit 5: final clinic visit (week 32)

With each of the clinic study visits, you will have the following clinical measures (vital signs) taken:

- height
- weight
- measurement of your waist and hips with a tape measure
- blood pressure

There will be a baseline lab visit, a 16-18 week lab visit, and a final study lab test visit. These visits will be scheduled before you start treatment (baseline), 16-18 weeks after starting treatment, and final visit after week 30 of treatment. During the baseline and final testing visits, you will take an oral glucose (sugar) tolerance test. For the sugar tolerance test to work, the night before the test you cannot eat anything after midnight and the only liquid you can drink after midnight is water. This test requires that blood samples be taken when you arrive, 30 minutes, 1 hour, and 2 hours after drinking a sugar solution to check your blood for glucose (sugar) and insulin. The first blood sample will also be used for laboratory tests of your hormones and blood chemistries. This blood test is to find out if your thyroid, liver, kidneys, and lipid levels are normal and to be sure you are not pregnant. In total, this test requires that you have your blood taken 4 times within 2 hours. The total amount of blood to be taken during each visit will be about 3 tablespoons. A total of 6 tablespoons of blood will be drawn during your taking part in this study.

At the 16-18 week visit, only a single blood sample (around 1 ½ teaspoons) will be drawn to confirm you are not pregnant and check your liver and kidneys. You will not need to be fasting.

You will also undergo a total of 2 whole body "DEXA" (dual energy X-ray absorptiometry) scans. These scans will be performed when you begin the study and at 32 weeks. These scans measure your body fat and lean tissue (this is like an x-ray machine).

In addition, you will keep a monthly calendar diary which we give to you to record when you have a menstrual bleeding (period) or spotting.

This drug is not approved for use by pregnant women. You will be asked to perform a home pregnancy test every month that we do not test your blood in the laboratory. The test kits will be provided to you at no cost. The study coordinator will make sure you remember to do the test each month by calling you for the result which will be documented in your chart. It

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is necessary that you not be pregnant while taking these medications. We need to make sure you are not pregnant every month you are in the study.

You will see the physician in the Metabolic Clinic before starting the medicine and at the end of the study. The clinic nurse will also see you about 16-18 weeks after starting the medication. These clinic visits are done to find out how you are tolerating the medicine, check your weight and blood pressure, look at your menstrual diary, and to give you new medicine and home pregnancy test kits.

A patient flow chart with a review of study visits is shown at the end of the consent form (Figure 1).

Risks/Side Effects

The treatments used in this study may cause some or none of the side effects listed. In addition, there is always the risk of some very uncommon or unknown side effects taking place.

Be sure to tell your physicians and pharmacist that you are taking one of these study medications. This is important so that they can tell you about any drug interactions that may exist with other medicines you may be taking.

Risks Associated with Study Procedures

Possible risks and side effects from each of these tests and drugs are listed below. Since you will need to have blood drawn from your arm several times, you may have some tenderness from having blood taken from a vein in your arm. The risks of drawing blood include local pain, bruising and swelling, bleeding, and infection at the site of the vein puncture. An infrequent risk of lightheadedness, dizziness, and, rarely, fainting is possible.

You will also have to take shots. There may be a risk of infection, mild injection-site bruising related to the injection (shot) method, and local reaction at the injection sites.

Risks Associated with Dual Energy X-ray Absorptiometry (DEXA) Scans for Body Composition

This is a painless test that is done on a "DEXA" machine (this is like an x-ray machine). The scan time is 180 seconds (3 minutes). The amount of radiation you will be exposed to from having this scan done is minimal. When the scan is performed, the x-ray exposure is 1.0 mrad, which is the same as about **1/30** the amount of x-ray exposure you would get from having a chest x-ray done.

Risks/Side Effects Associated with Study Medication

Liraglutide injection 3mg (Saxenda) has been approved by the U.S. Food and Drug Administration (FDA) for weight loss and ongoing weight management. This medicine should be used with a reduced calorie meal plan and increased physical activity. Liraglutide 3mg

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(Saxenda) is an injectable medicine used to help adults with excess body weight (BMI \geq 30) lose weight and keep the weight off. It comes in a prefilled injection (shot) pen (pen-injector) with fixed doses and uses a very small needle. This drug is given by subcutaneous (under the skin) shot in the thigh, abdomen, or upper arm.

You will need to take subcutaneous shots of liraglutide 3mg (Saxenda) or placebo Saxenda daily. There may be a risk of infection, mild injection-site bruising related to the injection (shot) method, and local reaction at the injection sites. Women treated on this study will be encouraged to rotate the site of the shot to avoid local reaction.

Possible risks from the study medicine are listed below:

Liraglutide 3mg (Saxenda) is a peptide (small protein) and therefore cannot be given by mouth. If it were taken in pill form, your stomach would break it down just like the protein in the foods you eat, and it wouldn't work. If you miss a dose, skip that dose and restart your therapy with the next scheduled dose. Liraglutide 3mg (Saxenda) should be refrigerated (36-46 °F) until you use the first dose and protected from light. The product should not be used if it has been frozen. The pre-filled pen should be thrown away 30 days after first use.

Your treatment will start at a low dose which will gradually be increased over the first 5 weeks of treatment. Treatment will be started at a dose of 0.6 mg given the same time each day for 1 week. After 1 week, the dose of Saxenda or placebo should be increased to 1.2 mg daily. You should increase your dose by 0.6 mg each week (week 3=1.8 mg; week 4= 2.4 mg) until you reach the recommended dose of 3.0 mg once a day)

The most common side effects of Liraglutide 3mg (Saxenda) include

- | | |
|----------------------|---|
| • nausea | • headache |
| • vomiting | • feeling jittery |
| • dizziness | • upset stomach |
| • diarrhea | • changes in enzyme (lipase) levels in your blood |
| • constipation | |
| • decreased appetite | |

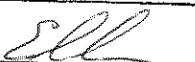
Nausea is most common when first starting Liraglutide 3mg (Saxenda), and as you increase your dose but decreases over time in most people as their body gets used to the medicine. If needed, the study doctor can provide a prescription for medicine to help with the nausea.

Less common side effects include:

- tiredness
- indigestion
- increased heart rate

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Tell the study doctor if you have any side effect that bothers you or does not go away.

Any drug may cause serious side effects, including **serious allergic reactions**. Since this drug is a peptide, the potential to develop antibodies to liraglutide 3mg (Saxenda) following treatment with liraglutide 3mg (Saxenda) exists. **Some signs of allergic reactions are:**

- skin rash
- fever
- fast pulse
- sweating
- swelling around mouth, throat or eyes

If not treated quickly, more serious problems such as breathing difficulties or shock could occur. It is not possible to predict if any of these problems will develop. If you have a serious allergic reaction, you may be at risk of death if not treated. Please seek treatment and alert the study doctor and staff right away if you have any of these signs or any other side effects during the study.

Low blood sugar (hypoglycemia) is a possible side effect to consider when taking liraglutide 3mg (Saxenda). **Liraglutide 3mg (Saxenda) alone does not cause low blood sugar** but it has been shown to cause hypoglycemia when used with other anti-diabetes drugs. **The warning signs of low blood sugar may include:**

- headache
- drowsiness
- weakness
- dizziness
- confusion
- irritability
- hunger
- fast heartbeat
- sweating
- feeling jittery

You will be trained how to recognize the signs of low blood sugar, and what to do to treat it. It is a good habit to carry glucose (sugar) tablets or gel to treat low blood sugar. If you don't have these forms of glucose, eat a quick source of sugar such as table sugar, honey, or candy, or drink a glass of orange juice or non-diet soda to quickly raise your blood sugar level. Tell your doctor right away about the reaction.

Serious side effects may happen in people taking liraglutide 3mg (Saxenda) including:

Liraglutide 3mg (Saxenda) causes thyroid C-cell tumors in rodents (mice and rats). The human relevance is unknown. You should tell the study doctor if you experience any symptoms of a thyroid tumor (e.g. a mass in the neck, difficulty swallowing, shortness of breath, or persistent hoarseness).

Cases of inflammation of the pancreas (pancreatitis) have been reported uncommonly in patients using Saxenda. Pancreatitis is a serious, potentially life-threatening medical condition. Stop taking Saxenda and contact a doctor immediately if you notice any of the following side effects: severe and persistent pain in the abdomen (stomach area) that will not go away, with or without vomiting. You may feel the pain from your abdomen through to your back.

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Liraglutide 3mg (Saxenda) may cause gallbladder problems, including gallstones. Some gallbladder problems need surgery. Call your doctor if you have any of the following symptoms: pain in your upper abdomen (stomach), fever, jaundice (yellowing) of your skin or eyes and clay-colored stools.

Liraglutide 3mg (Saxenda) should be used with care if you are taking oral medicines that require rapid absorption through your stomach. Liraglutide 3mg (Saxenda) slows stomach emptying and can affect medicines that need to pass through the stomach quickly. Liraglutide 3mg (Saxenda) can interact with other medicines. Drugs that depend on a threshold concentration to be effective, such as antibiotics, should be taken at least one hour before Liraglutide 3mg (Saxenda) shot.

Liraglutide 3mg injection (Saxenda) can interact with other medicines. Know the medicines you take including prescription and non-prescription drugs, vitamins, and herbal supplements. Keep a list of them to show the study doctor or study staff throughout the time you are taking part in this research study.

If any new risks or side effects are found out that might change your decision to stay in this study, you will be told about it in a timely manner.

Pregnancy

The FDA has created guidelines for drug companies to follow in regards to labeling medications and their impact on pregnancy. The FDA has assigned pregnancy category X to liraglutide injection 3mg (Saxenda). **The treatment might harm an unborn child; therefore you should not take part in this study if you are pregnant, breast feeding or you may become pregnant during the study period.** If you can become pregnant (unless sterilized), you will need to have a negative pregnancy test (blood or urine) before taking Saxenda and take a pregnancy test every month while taking Saxenda. You also must agree to use a reliable form of contraception consistently during the trial (e.g., intra-uterine device (IUD), diaphragm with spermicide plus condom). This should be continued for at least 1 month after the treatment has finished.

Patients in all treatment groups will have the same tests done. You will be required to be using contraception (unless you have been sterilized) in order to participate in the study. This contraception method must be maintained during the study. Do not use any of the study medications without telling your doctor if you are breast-feeding a baby. It is not known whether any of the study drugs pass into breast milk or if they could harm a nursing baby.

Any treatment can cause side effects. The drugs used in this study may cause some or none of the side effects listed. This study may also have risks not known at this time. There is always the risk of some very uncommon or unknown side effects occurring which have not been explained in this consent. Risks to subjects are minimized by using procedures consistent

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with sound research dosing. In addition, a listing of other known side effects of both drugs is on hand through the pharmacy or from the drug company.

If you do not understand any of the risks you may discuss them with Dr. Harris, Dr. Bellanger, or Dr. Elkind-Hirsch. Although the risks of developing the above complications are small, they do exist. If they occur, Dr. Harris, Dr. Bellanger, or Dr. Elkind-Hirsch and their team will watch you closely and take appropriate medical action. This may include stopping the use of the drug. Your primary care physician is still responsible for your medical care.

Benefits

As a result of taking part in the study, you will receive medical care. You will be checked throughout the study. The medicine in this study has been used in adults with excess body weight and has been shown to result in significant weight loss. However, this benefit cannot be certain in women with PCOS. It is possible that you may not receive any benefit from this study. Society will gain from learning if the use of the weight loss medicine liraglutide 3mg (Saxenda) has a positive effect on weight loss, body composition and reproductive function in women with PCOS.

Alternative Treatment

Caloric restriction and exercise are alternative methods that are used to reduce excess weight. A number of approved weight loss drugs are another choice that may be right for you. You may talk over the use of these with your primary health care professional or the health care professionals in this study. You do not need to take part in this study to receive treatment for your condition.

Costs

There will be no charge for any of the study measurements or blood tests. All study medication and exams will be provided free of charge throughout the time you are in this trial. Test results will be offered to you as well as your private doctor(s) if you give separate written consent for information to be sent to your doctor(s). You will get \$100 after study baseline screening and \$100 after the last study testing visit (in which you have a 2-hour lab test at the hospital) and see the physician to pay for local travel, meals, and other costs from your study visit. Your health insurance company or you will pay for all other costs associated with your medical care. Woman's Hospital will be given payment from the study sponsor to cover some of the costs for carrying out the study and data collection.

Confidentiality

The results of this study may be published. Your name and identity will be kept private. Every effort will be made to keep your study information confidential. Absolute confidentiality cannot be guaranteed. Your study records will be part of your medical chart. Your study chart will be kept in a locked filing cabinet. Your study chart and study data will be kept for a minimum of three years. An agent from NovoNordisk, the company supplying the medicine, may look at your records. The data will not be shared with other researchers. The Woman's

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Hospital Foundation Institutional Review Board, Woman's Hospital Research and Development Committee, research and clinical study staff, as well as Woman's Health Research Department, and the Food and Drug Administration may also check your study records.

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Contacts for Extended Medical Care

If an injury happens while you are taking part in this study, medical care will be given to you. No funds have been set aside to pay your costs in the event of an injury as a result of this study. If an injury does occur, medical care can be gotten easily. The cost of this medical care will be the responsibility of you and/or your insurance company.

If you are hurt while taking part in this study, you should contact the Woman's Metabolic Clinic at (225) 924-8947. For more information about this research or patients' rights in research, you may also contact Ericka Seidemann, Human Protections Administrator, at (225) 231-5296.

Termination of Participation

At any time, you may ask that your test results not be used for research. Your decision to not take part will not have a penalty. You can leave the study at any time without changing your further care. Please call Dr. Elkind-Hirsch at (225) 231-5278 if you no longer wish to take part in the study. The researchers may need to stop your taking part in the study for any of the following reasons:

- you become pregnant
- an adverse event that leads to stopping of treatment by your physician
- you develop a related sickness, which increases the risk to you or halts the analysis of the study facts
- you have to take an unacceptable medicine at the same time
- not following study instructions
- finding out that you are not eligible
- new information about the study drug is discovered that may affect your wish to continue taking part
- the study doctor feels it is in your best interest

Acknowledgement Of Receipt Of Information And Consent To Participate

I HAVE HAD AMPLE OPPORTUNITY TO ASK ANY QUESTIONS CONCERNING THE STUDY AND MY PARTICIPATION IS VOLUNTARY AS REFLECTED BY THE SIGNED STATEMENT BELOW.

I have read the preceding description and have heard the verbal explanation of these procedures from my doctor. I freely give my consent to participate in this research. I have the

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right to ask questions and may refuse to continue in the study any time. If I refuse to participate or if I withdraw from the study, the doctors will continue to care for me and treat me as necessary for my condition.

During the course of the research study, I will be informed of any new significant findings that may relate to my willingness to continue to participate.

At any time during treatment I am free to discuss with my doctor or his/her designee or the WHF Human Protections Administrator my rights as a participant and any side effects that might occur.

I AM MAKING A DECISION WHETHER OR NOT TO PARTICIPATE IN THIS STUDY. MY SIGNATURE INDICATES THAT I HAVE DECIDED TO PARTICIPATE, HAVE READ (OR BEEN READ) THE INFORMATION PROVIDED HEREIN, AND THAT I HAVE RECEIVED A COPY OF THIS INFORMED CONSENT FORM.

Patient Name	Date
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Patient Signature	Date
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Signature of Person Administering Consent	Date
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Investigator Signature	Date
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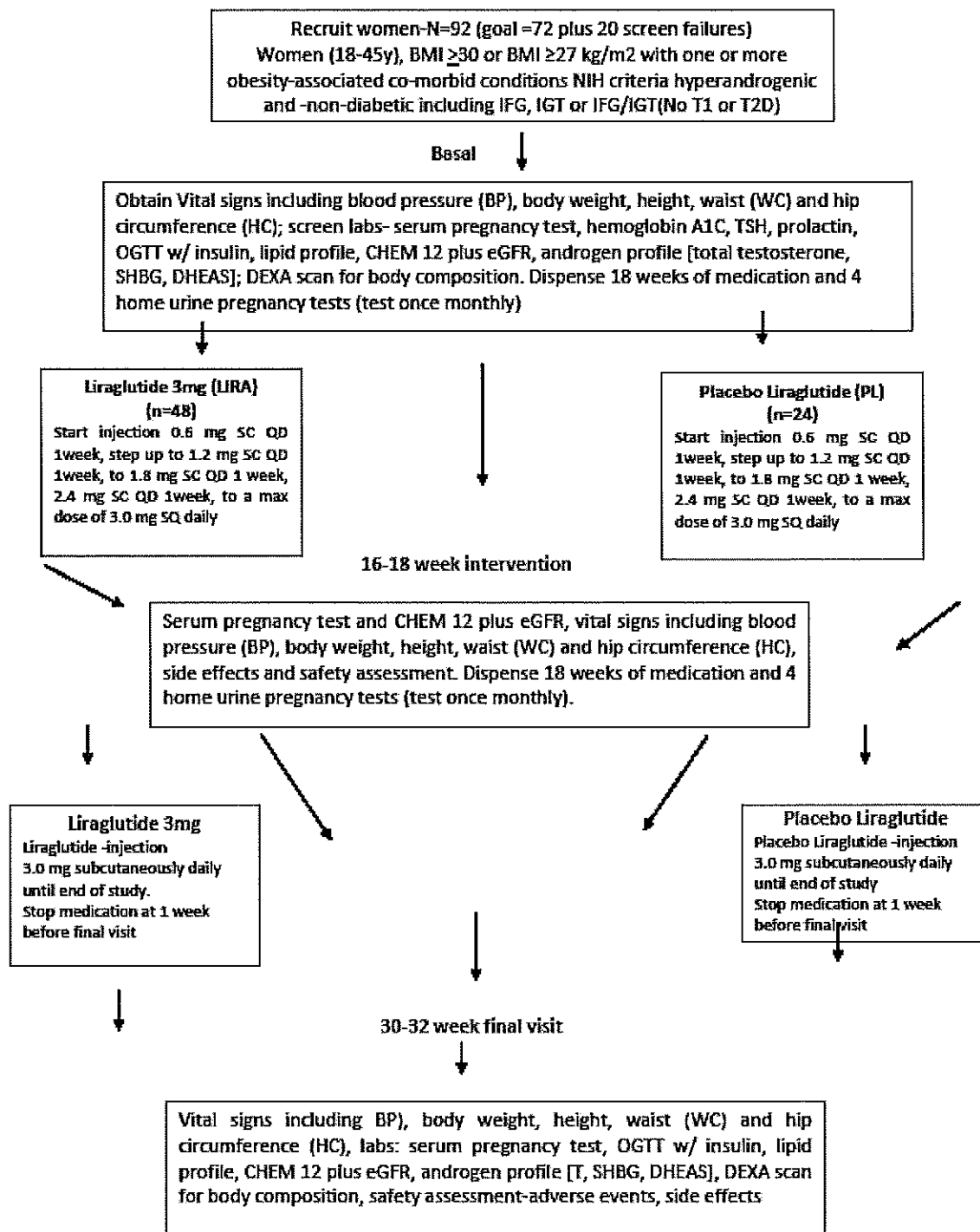
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Figure 1: Flow of Patients Through Trial

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